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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/828,837	04/21/2004	Richard L. Gregory	7037-486	5846

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EXAMINER
CHOWDHURY, IQBAL HOSSAIN

ART UNIT	PAPER NUMBER
1652	

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DATE MAILED: 12/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/828,837	GREGORY ET AL.	
	Examiner	Art Unit	
	Iqbal Chowdhury, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *2,4,8-15 and 18-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5-7,16 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/29/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a CIP of 10/009,004 ABN, which is a 371 of PCT/US00/11992 filed on 4/21/2004.

Claims 1-42 are pending and are present for examination.

Applicant's election with traverse of Group I (claims 1-7, 16 and 17) and the invention A (SEQ ID NO: 6), drawn to a method of controlling dental plaque in the oral cavity of a host by using polypeptide murein hydrolase in the response filed on 10/3/2005 is acknowledged.

The traversal is on the ground(s) that there would be no burden of search for the coexamination of all the groups I-V simultaneously. This is not found persuasive because while the search necessary for examination of all the groups overlaps it is not coextensive, examination of Group I-V would require search of subclasses unnecessary for the search of Group I, for example 424/94.6; 424/50; 435/259; 435/195 and 536/23.2, and inventions (A)-(B). As restriction is clearly permissible even among related inventions as defined in MPEP 808 and 35 U.S.C. 121 allows restriction of inventions, which are independent or distinct.

Applicants also argue that all the claims are closely related by a common enzyme murein hydrolase or murein hydrolase activity or sequences encoding murein hydrolase, which is not persuasive as restriction is clearly permissible even among related inventions as defined in MPEP 808.

Applicant's further argue that SEQ ID NO: 6 and 8 both recites molecules that encode hydrolase activity. This is not persuasive because contrary to applicants arguments, SEQ ID NO:

6 encoding a protein of 335 amino acid where as SEQ ID NO: 8 encoding a protein of 611 amino acid, which are structurally different and expected having different rate of activity and a search for each of the sequences would not be done solely by searching electronic sequence databases as such databases seldom provide extensive coverage of all variants or mutants which are known or have been made of a single protein such that word searching for each variants or mutants is required. Furthermore, even sequence searching of the 2 different proteins would be a substantial burden on the office, as each sequence has to be examined individually to determine if it includes any variants or mutants. As such the novelty and non-obviousness of each variants or mutants would have to be addressed individually creating a large burden on the office.

The requirement is still deemed proper and is therefore made FINAL.

Claims 2, 4, 8-15 and 18-42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Note claim 2 has been withdrawn as the molecular weight recited corresponds to that of the non-invention (i.e. SEQ ID NO: 8) and not the molecular weight of the elected invention (i.e. SEQ ID NO: 6). Applicant timely traversed the restriction (election) requirement in communication filed on 10/3/2005.

Claims 1, 3, 5-7, 16 and 17 are under consideration and are being examined herein.

Claim Objections

Claim 1 is objected to, as the recitation "a polypeptide having S. mutans murein hydrolase activity" should be "a polypeptide having murein hydrolase activity isolated from S. mutans". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 16 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims 16 and 17 are indefinite in the recitation "at least about 70%" which is ambiguous and confusing. It is unclear what applicant meant by "at least about 70%".

Claims 3 and 16-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 3 and 16-17 are indefinite in reciting "murein hydrolase having a molecular weight about 65 kDa and an amino acid sequence having at least 70% identity to SEQ ID NO: 6" which is ambiguous and confusing. The protein of SEQ ID NO: 6 is 335 amino acids in length such that its molecular weight cannot be 65 kDa as claimed. For examination purposes claim 2 has been withdrawn as drawn to non-elected invention, claim 3 is examined as if dependent on claim 1, and "having a molecular weight of about 65 kDa" in claim 16 will be given no patentable weight.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 5-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a method of controlling dental plaque in the oral cavity of a host using a genus of protein molecule encoding any polypeptide murein hydrolase. The specification teaches the structure of only two representative species of such proteins. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of murein hydrolase activity. Given this lack of description of representative species encompassed by the genus of protein molecule used in the methods of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 1, 3, 5-7 and 16-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of using murein hydrolase from S. mutans of SEQ ID NO: 6, does not reasonably provide enablement for methods of using any murein hydrolase or any polypeptide having 70% identity to SEQ ID NO: 6. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1, 3, 5-7 and 16-17 are so broad as to encompass methods for controlling dental plaque in the oral cavity of a host using a genus of protein molecule encoding any polypeptide murein hydrolase (claims 1 and 5-7) or any murein hydrolase or polypeptide having 70% identity to SEQ ID NO: 6 (claims 3, 16 and 17). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of murein hydrolases broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only two murein hydrolases.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple point mutations or substitutions.

The specification does not support the broad scope of the claims which encompass methods for controlling dental plaque by using any murein hydrolase because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting murein hydrolase activity; (B) the general tolerance of murein hydrolase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any murein hydrolase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including methods of using any murein hydrolase or any murein hydrolase having 70% identity to SEQ ID NO: 6. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of murein hydrolase to use in the claimed methods having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 16-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a method of controlling dental plaque in the oral cavity of a host using a genus of protein molecules of SEQ ID NO: 6 or any protein, which is 70% identical to SEQ ID NO: 6. The specification does not contain any disclosure of the function of all protein sequences that are 70% identical to SEQ ID NO: 6. The genus of protein molecule having more than 70% identity to SEQ ID NO: 6 comprise many different proteins or mutants or variants having many diverse functions. Therefore, many functionally unrelated proteins are encompassed within the scope of these claims. The specification discloses only two species of the claimed genus, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 and 5-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Kim et al. ("Purification and properties of bacteriolytic enzymes from Bacillus licheniformis YS-1005

against Streptococcus mutans", Biosci Biotechnol Biochem. 1999 Jan; 63(1): 73-7). Kim et al. teach an isolation of an enzyme, which is similar to murein hydrolase, or peptidoglycan amidohydrolase, which has lytic activity against cariogenic Streptococci mutans. Kim et al. also purified the protein and assayed the lytic activity against many bacterial species in terms of lysis of the bacteria including S. mutans. Kim et al. further teach that the enzyme is most effective against S. mutans, which is the main causative agent of dental caries and the enzyme digest the peptide linkage between L-Ala and D-Glu in peptidoglycan of Streptococcus mutans. The lytic activity was highly specific for Streptococcus mutans, suggesting their potential use as a dental care product.

Claim 1, 3 and 5-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Gregory et al. (WO00/66616, "Methods and compositions for controlling dental caries, and recombinant smaA polypeptides useful for same", see IDS). Gregory et al. teach an isolation of a gene encoding a protein smaA from Streptococcus mutans, which sequence is 100% identical to SEQ ID NO: 6 and thus inherently a murein hydrolase. Gregory et al. also disclose the use of this protein for controlling dental caries. Gregory et al further disclose the cloning and expression of said protein in host cell and produced recombinant protein. While Gregory et al. was published after the filing date of the applications to which applicants claim priority neither PCT/US00/11992 nor 60/132312 provide support for the recitation of "having murein hydrolase activity " in claim 1. As such claims 1, 3 and 5-7 have not been granted the benefit of the filing date of the prior applications.

Literature of Interest

Ogier et al. "A 40-kilodalton cell wall protein-coding sequence upstream of the sr gene of

Streptococcus mutans OMZ175 (serotype f)", Infect Immun. 1991 May; 59(5): 1620-6.

GenBank accession No. A60328, "40K cell wall protein precursor (sr 5' region) – Streptococcus mutans (strain OMZ175, serotype f), created 2/20/1993.

Conclusion

Status of the claims:

Claims 1, 3, 5-7, 16 and 17 are pending.

Claims 1, 3, 5-7, 16 and 17 are rejected.

No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

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